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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,168	02/09/2006	Luigi Aurisicchio	ITR0058P	4577

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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03/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,168	AURISICCHIO ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,19 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,19 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/06;12/3/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I (Claims 1, 6-9, 15, 16 and 19) in the reply filed on December 3, 2007, is acknowledged.

2. Applicant's preliminary amendment filed on December 3, 2007, is acknowledged. Claims 2-6, 10-18 and 20-29 have been cancelled. New Claim 30 is added.

3. Accordingly, Claims 1, 7-9, 19 and 30 are pending and are considered in this Office action.

Information Disclosure Statement

4. The information disclosure statements submitted on February 9, 2006, and December 3, 2007, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner. The initialed and dated copies of Applicant's IDS form 1449 are attached to the instant Office action.

Claim objection

5. Claim 19 is objected to because the term "wherein the polynucleotide comprises **a** sequence of nucleotides as set forth in SEQ ID NO: 1" encompasses nucleic acids that comprise any portion of SEQ ID NO: 1, for example, as small as a dinucleotide or larger oligonucleotide. To be consistent with the claim limitation "a polynucleotide encoding a rhesus monkey CEA protein," the wherein clause is suggested to amend to "wherein the polynucleotide comprises **the** sequence of nucleotides as set forth in SEQ ID NO: 1".

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

7. Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 8 reads on a host cell comprising a vector of a codon-optimized CEA gene. However, since the claim does not require an isolated cell, the claim reads on a human being that comprises a cell containing a codon-optimized CEA gene. Products of nature, like a human being, do not constitute patentable subject matter under 35 U.S.C. § 101. Amending the claim to "an isolated host cell" would overcome this rejection.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 7-9, 19 and 30 are rejected under 35 U.S.C. 103(a) as being obvious over Aurisicchio (WO 22204/072287, priority date: 60/447,203 filed on February 2003), in view of in view of Nagata (Biochem Biophys Res Commun. 1999 Aug 2;261(2):445-51) and Kotsopoulou (J. Virology 74(10):4839-4852, 2000).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C.

102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

10. Claims 1, 7, 8, 19 and 30 are drawn to a synthetic nucleic acid molecule, a vector and a host cell that comprise a nucleotide sequence that encodes rhesus monkey carcinoembryonic antigen (rhCEA) protein, wherein the nucleotide sequence is codon-optimized for high level expression in a human cell, wherein the nucleotide sequence comprises SEQ ID NO: 1, and wherein the vector is an adenovirus vector. Claim 9 is drawn to a process for expressing a rhCEA protein using the nucleic acid of Claim 1.

11. Aurisicchio (WO 22204/072287) teaches a rhCEA gene and a vector that encodes the rhCEA protein SEQ ID NO: 2 (Abstract, pp. 2 and 3 and claims). Aurisicchio also teaches that rhCEA gene is inserted into an adenoviral vector (p. 13-15 and Example 4). The sequence alignment indicates that the protein product of the instant nucleotide SEQ ID NO: 1 is a rhCEA

protein, whose amino acid sequence is 100% identical to the rhCEA protein SEQ ID NO: 2 of Aurisicchio (WO 22204/072287).

12. Aurisicchio (WO 22204/072287) does not explicitly teach the codon-optimized rhCEA gene SEQ ID NO:1.

13. Nagata provides teaching indicating that codon-optimized gene encoding CTL epitopes with mammalian cell-preferred codons increases the translational efficiency of the gene in mammalian cells, which increases CTL responses in BALB/c mice (Abstract, p. 449 and Figures 2 and 3).

14. Kotsopoulou shows that codon optimized HIVgag-pol gene results in a 10-fold increase in steady-state levels of cognate RNA with a concomitant 10-fold increase in protein production (Left col., p. 4844, Figs. 2 and 3, and Para 3, right col., p. 4848). Kotsopoulou teaches that codon optimization can be achieved with the help of codon usage tables, see e.g. Table 1.

15. It would have been obvious to one of ordinary skill in the art to make a codon-optimized rhCEA gene SEQ ID NO: 1 in order to increase the expression of rhCEA gene in human cells. One would have been motivated to do so and have a reasonable expectation of success that the codon-optimized rhCEA gene would have better expression in cells, given the knowledge that the codon-optimized virus gene can significantly increase its RNA transcription and translation level in human cells, as taught by Nagata and Kotsopoulou, given the knowledge of the rhCEA gene sequence is available, as disclosed by Aurisicchio (WO 22204/072287), and given that codon optimization can be achieved with the help of codon usage tables, as taught by Kotsopoulou. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 1, 7-9, 19 and 30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the allowed Claims 1, 5-8, 11, 15-18 and 35-40 of co-pending application 10/545,515 ('515). Although the conflicting claims are not identical, they are not patentably distinct from each other because Claims 1, 7-9, 19 and 30 of the instant application are obvious variations of the invention defined in the co-pending application '515, in view of Nagata (Biochem Biophys Res Commun. 1999 Aug 2;261(2):445-51) and Kotospoulou (J. Virology 74(10):4839-4852, 2000).

17. Claims 1, 7, 8, 19 and 30 of the instant application are drawn to a synthetic nucleic acid molecule, a vector and a host cell that comprise a nucleotide sequence that encodes rhesus monkey carcinoembryonic antigen (rhCEA) protein, wherein the nucleotide sequence is codon-optimized for high level expression in a human cell, wherein the nucleotide sequence comprises

SEQ ID NO: 1, and wherein the vector is an adenovirus vector. Claim 9 is drawn to a process for expressing a rhCEA protein using the nucleic acid of Claim 1.

18. Claims 1, 5-7, 11, 15-18 and 35-40 of co-pending application '515 are drawn to a nucleotide, a vector and a host cell that comprise a rhCEA gene, which encodes rhCEA protein sequence SEQ ID NO: 2 or SEQ ID NO: 8, wherein the vector is an adenovirus vector, wherein the adenovirus vector is an Ad5 or an Ad6. Claim 8 is drawn to a process for expressing rhCEA protein using the nucleic acid of Claim 1.

19. The sequence alignment indicates that the protein product of the instant SEQ ID NO: 1 is a rhCEA protein, whose amino acid sequence is 100% identical to the rhCEA protein SEQ ID NO: 2 of co-pending application '515 (Claim 1), and 99% identical to rhCEA protein SEQ ID NO: 8 of co-pending application '515 (Claim 11). Since the instant SEQ ID NO: 1 encodes a rhCEA protein that is the same or substantially the same as those of '515, the instant SEQ ID NO: 1 is another form (or variation) of the rhCEA genes of '515.

20. Furthermore, although the copending application '515 does not teach the instant codon-optimizd rhCEA gene, SEQ ID NO: 1, it is known in the art that codon-optimization is a standard molecular biology strategy for improving gene expression in human cells, for example, increasing an antigen expression by DNA vaccine in human cells (See e.g. Nagata, Abstract and Par 2, right col. p. 445; and See, e.g. Kotsopoulou). The codon optimization can be achieved with the help of codon usage tables and a codon usage database (See, e.g. Kotsopoulou, Table 1 and p. 4841). Therefore it would have been obvious to one of ordinary skill in the art to optimize the rhCEA gene sequence of '515 in order to increase the gene expression of rhCEA in human cells.

21. Given that the rhCEA protein encoded by the instant SEQ ID NO: 1 is the same or substantially the same as those of the co-pending application '515, given that the codon-optimized gene SEQ ID NO: 1 is another sequence form of rhCEA gene manipulated for improving gene expression in human cells, the subject matter of the instant claims is obvious over Claims 1, 5-8, 11, 15-18 and 35-40 of co-pending application '515, in view of Nagata and Kotospoulou.

Remarks

22. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Bo Peng/
March 12, 2007